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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/698,341

10/27/2000

Joseph A. Sorge

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05/07/2002

PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS / STR
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER

HUTSON, RICHARD G

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 05/07/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/698,341

Applicant(s)

SORGE ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 January 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-10,12-47 and 85-88 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-3,5,46 and 47 is/are allowed.
- 6) ☐ Claim(s) 6-10 and 12-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants cancellation of claims 4, 11, and 48-84 without prejudice, the amendment of claims 6, 10, 12 and 14 and the addition of claims 85-88 is acknowledged. Claims 1-3, 5-10, 12-47 and 85-88 are at issue and present for examination.

Specification

The disclosure is objected to because of the following informalities: Page 23, line 5, recites "...the conventional deoxynucleotides dATP, dCTP, dGTP and TTP..." It is believed that applicants intended that "TTP" be "dTTP". Applicants response to this suggestion and applicants presentation of the sigma catalog to support their assertions is noted. However, applicants argument is not persuasive. It is noted that applicants have presented the Sigma catalog listing of the compound, "Thymidine 5'-Triphosphate" not a deoxynucleotide, which is the compound of the objected to recitation. Applicants attention is further directed to page 72 of Stryer, Biochemistry, Third Edition, 1988, W.H. Freeman and Co., New York, which teaches "The four nucleoside units in DNA are called deoxyadenosine, deoxyguanosine, **deoxythymidine**, and deoxycytidine. ...For example, deoxyadenosine 5'-triphosphate (dATP) is an activated precursor in the synthesis of DNA....The prefix *d* in ATP indicates that the sugar is deoxyribose to distinguish this compound from ATP, in which the sugar is ribose." The objection is further maintained to provide consistency in the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The rejection is stated in the previous office action.

Applicants traverse this rejection on the basis that the Thermococcus strain JDF-3 is not essential to the claimed invention and applicants have provided polynucleotide and amino acid sequences for wildtype JDF-3 polymerase and specified sites and substitutions for a number of mutants satisfying the limitations of claims 6-15 and finally that this is all that is required to satisfy the written description requirement. Applicants argument is not persuasive for the following reasons. While it is admitted that applicants do teach the Thermococcus strain JDF-3 polynucleotide and amino acid sequences in the specification and teach some substitutions which are encompassed by the currently rejected claims, the claims do not recite any specific polynucleotide or amino acid sequences and thus claims to a Family B DNA polymerase from Thermococcus species JDF-3 require the Thermococcus species JDF-3. While the

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claims are read in light of the specification, the specification is not limiting to the claims.

If it is applicants intent that the claimed *Thermococcus* strain JDF-3 Family B DNA polymerase has a specific sequence corresponding to a specific SEQ ID NO:, then it is suggested that applicants amend the specification to include such a limitation, otherwise, the organism from which the polymerase is isolated, must be fully disclosed or shown to be publicly known and freely available. Accordingly, it is deemed that a deposit of this strain should have been made in accordance with 37 CFR 1.801-1.809.

Claims 6-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention..

The rejection was stated in the previous office action.

Applicants traverse this rejection on the basis that the application as a whole describes the claimed invention in terms that convey to one skilled in the art that Applicants were in possession of the claimed genus(es) at the time the patent application was filed. Applicants submit that contrary to the characterization in the previous office action, the specification describes species beyond simply *Thermococcus* JDF-3 polymerase mutated at specific residues of SEQ ID NO: 2 and support this assertion by submitting that they provide a list of 55 Family B polymerases, literature references, and accession numbers for sequence information for 17 different Family B polymerases. Applicants further submit that alignments and knowledge of conserved

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regions in a given Family B protein permits one to identify amino acids or regions as critical functional determinants and applicants have provided methodologies to assess the impact of a given mutation. Applicants are reminded that this rejection was not based on a lack of enablement, but rather a lack of written description and that while applicants have described a number of additional "Family B polymerases" and cited references which compare the sequences of many of these polymerases, applicants have not described mutations which result in the desired polymerase properties in addition to those referred to in the previous office action. Applicants attempt to provide examples of the disclosed species of the claimed genres is unclear based on it is not entirely clear to which claimed genus each species belongs and regardless the number of species taught remain insufficient to adequately describe the claimed genres. For instance, applicants submit that the specification describes 25 mutant clones of exo⁻ JDF-3 Family B DNA polymerase (representing at least 4 different individual mutations covering both Regions II and III) and their relative nucleotide discrimination. To which of the claimed genres do each of these 25 mutant clones belong. Regardless, these are still insufficient to adequately describe the claimed genres drawn to all possible Family B DNA polymerases from *Thermococcus* species JDF-3 DNA that are 3' to 5' exonuclease deficient (claims 6-9, 12-15 and 17-21), all recombinant DNA polymerases having a reduced discrimination against non-conventional nucleotides (claims 16 and 22-45) and all recombinant DNA polymerases having a reduced discrimination against non-conventional nucleotides, wherein said DNA polymerase has a mutation in Region II (claims 10 and 85-87).

The specification only provides the representative species encompassed by these claims, wherein said mutant polymerase is from *Thermococcus* species JDF-3 and the mutation is selected from the group consisting of mutations at residues: S345, P410, D141, E143, A485 and L408, of SEQ ID NO: 2. While it is admitted that applicants disclose a number of mutations, these are not representative of the genus of mutations claimed which encompasses any and all mutations of any Family B or *Thermococcus* species JDF-3 DNA polymerase which results in a decrease in 3' to 5' exonuclease activity or a reduction in discrimination against non-conventional nucleotides. There is no disclosure of any particular structure to function/activity relationship in the claimed genuses. The specification also fails to describe additional representative species of these DNA Polymerase mutants by any identifying structural characteristics or properties other than having a decrease in 3' to 5' exonuclease activity or a reduction in discrimination against non-conventional nucleotides, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 14, 15, 16-45 and 85-88 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection was stated in the previous office action as it applied to claims 10-45.

Applicants traverse this rejection on the basis that the specification defines "non-conventional nucleotide" on page 25 of the specification as referring to "a) a nucleotide structure that is not one of the four conventional deoxynucleotides dATP, dCTP, dGTP and TTP, recognized by and incorporated by a DNA polymerase,..." Applicants further refer to a "non-conventional nucleotide" as "...or d) a ribonucleotide (since they are normally not recognized or incorporated by DNA polymerases) and modified forms of a ribonucleotide". While applicants submit that this definition makes it clear there are only four "conventional nucleotides", namely dATP, dCTP, dGTP and TTP. In light of the discussion above referring to the objection to the specification for reciting that TTP is a deoxynucleotide, applicants recited definition from the specification and applicants argument is not found persuasive. In response to applicants argument here and above and the confusion in the specifications reference to "TTP" as being a deoxynucleotide, this definition and claim remains unclear.

Claims 10 and 85-87 are indefinite in the recitation "Region II" as it is unclear what region of the claimed polymerase molecule corresponds to "Region II". It is

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unclear as to the metes and bounds of those amino acids which applicants consider are included in "Region II". Applicants submission that "The limits of the regions of the Family B DNA polymerases, including Region II are set out in Braithwaite and Ito and Wong et al. references (submitted Exhibits A and B) cited in the specification and incorporated in the specification by reference." is noted. However the incorporation of these references into the specification is improper because the definition of Region II of the claimed Family B polymerases is considered "essential material" to the claimed invention.

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112. Material nevertheless may be incorporated by reference, *Ex parte Schwarze*, 151 USPQ 426 (Bd. App. 1966). An application for a patent when filed may incorporate "essential material" by reference to (1) a U.S. patent, (2) a U.S. patent application publication, or (3) a pending U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112). In any application which is to issue as a U.S. patent, **essential material may not be incorporated by reference to** (1) patents or applications published by foreign countries or a regional patent office, (2) **non-patent publications**, (3) a U.S. patent or application which itself incorporates "essential material" by reference, or (4) a foreign application.

Claim 88 is indefinite in that it is unclear if applicants recitation of "JDF-3 DNA polymerase" is the same as a "Family B DNA polymerase from *Thermococcus* species

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JDF-3". As applicants do not have support for JDF-3 polymerases other than "Family B DNA polymerases from *Thermococcus* species JDF-3", this is how the claim is interpreted.

Claim Rejections - 35 USC § 102

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 10, 11, 14, 15, and 44 are rejected under 35 U.S.C. 102(e) as being anticipated by Riedl et al. (U.S. Patent No: 5,882,904, filed 8/4/1997).

The rejection is stated in the previous office action.

Applicants traverse this rejection on the basis that Riedl et al. does not teach an isolated Family B DNA polymerase having reduced discrimination against non-conventional nucleotides, wherein said DNA polymerase has a mutation in Region II as required by amended claim 10. Applicants submit that Riedl et al. teaches only *Thermococcus barosii* Family B DNA polymerase mutants bearing mutations in Region III, covering amino acids 488-493 and the exo mutation at amino acid 141 and 143 and that the reference does not teach any mutation in Region II.

Applicants argument is not found persuasive because applicants have not supported their assertions as to which region the mutations of Reidl et al. fall into (See above 112 2nd paragraph rejection).

C nclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

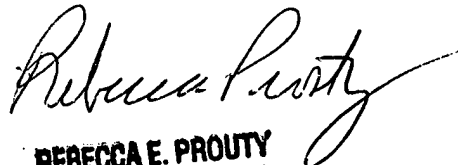
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson Ph.D.
Patent Examiner
Art Unit 1652
May 6, 2002


REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1800
1600